

XX
SQ Sequence 25 AA;
Query Match Best Local Similarity 100.0%; Score 132; DB 5; Length 25;
Matches 25; Conservative 0; Mismatches 0; Indels 0; Gaps 0;
Oy 1 NLWAQQRGRELRRMSDEFVDSFKK 25
Db 1 NLWAQQRGRELRRMSDEFVDSFKK 25

RESULT 2
ABP56161
ID ABR56161 standard; peptide; 25 AA.
XX
AC ABP56161;
XX DT 28-MAR-2003 (first entry)
XX DR PTPC-interacting TOX peptide #27.
XX KW Mitochondrial membrane permeabilisation; mitochondrion; PTPC;
KW permeability transition pore complex; viroicide; neuroprotective;
KW vasoconstrictive; cytostatic; infection; cell death regulation; apoptosis;
KW mitochondrial permeability transition pore complex modulator; cancer;
KW apoptogenic; ischaemia; neurodegenerative disease; fulminant hepatitis.
XX OS Synthetic.
XX PF 01-FEB-2002; 2002WO-EP001633.
XX PR 02-FEB-2001; 2001US-0265594P.
XX PA (INSP) INST PASTEUR
PA (CNRS) CENT NAT RECH SCI.
XX PI Edelman L, Jacotot E, Briand J;
XX DR WPI; 2002-619260/66.
XX PT New chimeric bi-functional molecules that target specific cells and
PT regulate the apoptosis function of the permeability transition pore
PT complex of the mitochondria, useful for treating or preventing e.g.
PT cancer or ischemia.
XX PS Claim 9; Page 11; 76pp; English.

The present invention describes a chimeric bifunctional molecule (I) comprising at least a first functional molecule covalently linked to a second functional molecule, which is able to modulate the activity of the permeability transition pore complex (PTPC) of the mitochondria. (I) has the ability of specifically targeting and entering a tissue cell population. The second functional molecule has the function of specifically targeting, and inducing or preventing the death of the cells comprising (I). (I) is useful for treating or preventing a pathological infection or disease. (I) is also useful for regulating cell death regulatory molecules, specifically the apoptosis by regulating the opening or closing of the PTPC of the mitochondria or its fragment. (I) has virucide, neuroprotective, vasoconstrictive and cytostatic activities, and can be used as a mitochondrial permeability transition pore complex (PTPC) modulator. (I) is useful for treating or preventing a pathological infection or disease. (I) is also useful for regulating cell death regulatory molecules, specifically the neurodegenerative diseases, fulminant hepatitis or viral infections. The present sequence represents a PTPC-interacting TOX peptide which is given in the exemplification of the present invention

XX SQ Sequence 25 AA;

Seq 20 NO = 10

Exhibit A

Best Local Similarity 100.0%; Pred. No. 3.4e-13; Matches 25; Conservative 0; Mismatches 0; Indels 0; Gaps 0;
Oy 1 NLWAQQRGRELRRMSDEFVDSFKK 25
Db 1 NLWAQQRGRELRRMSDEFVDSFKK 25

RESULT 3
AU78610
ID AAU78610 standard; peptide; 25 AA.
XX AC AAU78610;
XX DT 18-JUN-2002 (first entry)
XX DE Human Bad peptide #10 which binds to a member of the Bcl-2 family.
XX PN WO200220568-A2.
XX KW Human; Bad; Bcl-2; apoptosis; cancer; inducer; degenerative disease;
KW ischemic injury; suppressor; BH3 domain.
XX OS Homo sapiens.
XX PI Resik SW, Meadows RP, Joseph MK, Olejniczak ET, Petros AM;
Nettesheim DG, Swift KM, Matayoshi E, Zhang H;
DR WPI; 2002-292254/33.

04-SEP-2001; 2001WO-US027410.
06-SEP-2000; 2000US-00656399.

(ABBO) ABBOTT LAB.

XX PI Resik SW, Meadows RP, Joseph MK, Olejniczak ET, Petros AM;
Nettesheim DG, Swift KM, Matayoshi E, Zhang H;
DR WPI; 2002-292254/33.

New derivatives of Bad peptide, useful for identifying compounds that bind to Bcl-2 proteins, potential agents for treating cancer and degenerative disease.

Claim 18; Page 18; 31pp; English.

The present invention relates to new peptides that are derived from a wild-type human Bad peptide and are able to bind to a member of the Bcl-2 protein family. The peptides are useful, when labelled, in competitive/displacement assays for identifying substances that bind to members of the Bcl-2 family and may induce or suppress apoptosis so are potentially useful for treating cancer (inducers) or degenerative diseases or ischemic injury (suppressors). The peptides of the invention have high helix propensity, maintain the contacts of the wild-type Bad peptide and, compared with the Bad peptide, may have better physical properties, particularly solubility. The present sequence represents one of a collection of Bad peptides (AU78610-AAU78631) that were derived from the BH3 domain of the human wild-type Bad Peptide

XX SQ Sequence 25 AA;

Query Match Best Local Similarity 100.0%; Score 132; DB 5; Length 25;
Matches 25; Conservative 0; Mismatches 0; Indels 0; Gaps 0;
Oy 1 NLWAQQRGRELRRMSDEFVDSFKK 25
Db 1 NLWAQQRGRELRRMSDEFVDSFKK 25

RESULT 4
AU90776
ID ADK90776 standard; peptide; 25 AA.
AC ADK90776;

RESULT 2
US-08-717-123-2
Sequence 2, Application US/08171123

Patent No. 5965703
GENERAL INFORMATION:

APPLICANT: Horne, William A.
APPLICANT: Olterdorff, Tilman
TITLE OF INVENTION: Human Bdn Polypeptides, Encoding Nucleic
ACIDS AND METHODS OF USE
NUMBER OF SEQUENCES: 15
CORRESPONDENCE ADDRESS:

ADDRESSEE: Campbell and Flores
STREET: 4370 La Jolla Village Drive, Suite 700
CITY: San Diego
STATE: California
COUNTRY: United States
ZIP: 92122

COMPUTER READABLE FORM:

MEDIUM TYPE: Floppy disk
COMPUTER: IBM PC compatible
OPERATING SYSTEM: PC-DOS/MS-DOS
SOFTWARE: Patentin Release #1.0, Version #1.25

CURRENT APPLICATION DATA:

APPLICATION NUMBER: US/08/717,123
FILING DATE: 20-SEP-1996
CLASSIFICATION: 435
ATTORNEY/AGENT INFORMATION:

NAME: Campbell, Kathryn A.
REGISTRATION NUMBER: 31,815
REFERENCE DOCKET NUMBER: PP-ID 1929

REFERENCE/DOCKET NUMBER: PP-ID 1929
TELECOMMUNICATION INFORMATION:

TELEPHONE: (619) 535-9001
TELEFAX: (619) 535-8949

INFORMATION FOR SEQ ID NO: 2:

SEQUENCE CHARACTERISTICS:

LENGTH: 168 amino acids
TYPE: amino acid
TOPOLOGY: linear

MOLECULE TYPE: protein

US-08-717-123-2

Query Match Score 132; DB 1; Length 168;
Best Local Similarity 100.0%; Pred. No. 7.9e-13; Mismatches 0; Indels 0; Gaps 0;
Matches 25; Conservative 0; MisMatch 0;

Qy 1 NLWAQARYGRRLRMSDEFVDSFKK 25
Db 103 NLWAQARYGRRLRMSDEFVDSFKK 127

RESULT 3
US-08-985-335-1
Sequence 1, Application US/08985335

Patient No. 6080847
GENERAL INFORMATION:

APPLICANT: Hillman, Jennifer L.
APPLICANT: Yue, Henry
APPLICANT: Lal, Preeti

APPLICANT: Shah, Purvi
APPLICANT: Corley, Neil C.

TITLE OF INVENTION: PROTEINS ASSOCIATED WITH CELL
NUMBER OF SEQUENCES: 9
CORRESPONDENCE ADDRESS:

ADDRESSEE: Incyte Pharmaceuticals, Inc.
STREET: 3174 Porter Dr.
CITY: Palo Alto
STATE: CA
COUNTRY: USA
ZIP: 94304

COMPUTER READABLE FORM:
MEDIUM TYPE: Diskette
COMPUTER: IBM Compatible
OPERATING SYSTEM: DOS

SOFTWARE: FastSEQ for Windows Version 2.0
CURRENT APPLICATION DATA:
APPLICATION NUMBER: US/08/985,335
FILING DATE: Filed Herewith

PRIOR APPLICATION DATA:
APPLICATION NUMBER:

FILING DATE:
ATTORNEY/AGENT INFORMATION:
NAME: Billings, Lucy J.
REGISTRATION NUMBER: 36,749
REFERENCE/DOCKET NUMBER: PF-0421 US

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COMPUTER READABLE FORM:
MEDIUM TYPE: Diskette
COMPUTER: IBM Compatible

OPERATING SYSTEM: DOS
SOFTWARE: FastSEQ for Windows Version 2.0
CURRENT APPLICATION DATA:
APPLICATION NUMBER: US/08/985,335
FILING DATE: Filed Herewith

PRIOR APPLICATION DATA:
APPLICATION NUMBER:
FILING DATE:
ATTORNEY/AGENT INFORMATION:
NAME: Billings, Lucy J.
REGISTRATION NUMBER: 36,749
REFERENCE/DOCKET NUMBER: PF-0421 US

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